REMARKS

Discussion of Claim Amendments

Claims 27, 28, 30, 35, 45, 51, and 53 have been amended to further sharpen the claim language and claims 54-57 have been added and are directed to embodiments of the invention. The basis for the amended claim language may be found within the original specification, claims and drawings. No new matter has been added.

The Examiner Interview

Applicants wish to thank Examiner Todd Ware for the courtesies extended to Xavier Pillai, one of Applicants' attorneys, during the interview held on March 11, 2003.

Discussion of the Rejections

Applicants respectfully traverse the rejections. It is well known in the art that a microemulsion for pharmaceutical use is a thermodynamically stable suspension of submicron-size droplets of an oil phase stabilized by a surfactant, the droplets being dispersed in an aqueous medium. A preconcentrate is not a microemulsion, but rather a microemulsion is formed from a preconcentrate when the preconcentrate is mixed with an aqueous medium. The term "microemulsion preconcentrate" means that the preconcentrate forms a microemulsion on mixing with an aqueous medium. As stated in the specification at page 2, lines 27-32,

> "Microemulsions are thermodynamically stable and optically transparent or opaque depending on the particle size of the emulsion. Microemulsions have a mean droplet size of less than 200 nm, in general between 20-100 nm. In contrast to conventional emulsions, the microemulsions are formed in the presence of an aqueous phase by self emulsification without any energy input. In the absence of water, this self emulsifying system (i.e., the preconcentrate) exists as a transparent-looking mixture of oil and surfactants in which a lipophilic drug is dissolved."

The specification further states at page 4, lines 4-16,

> ". . . this invention provides a pharmaceutical composition in the form of a self-emulsifying preconcentrate comprising an anticancer drug as the active ingredient solubilized in a carrier medium comprising at least one hydrophobic component, at least one hydrophilic component and at least one surfactant. The . . . preconcentrates of the invention consist of a hydrophobic component, an

ingredient selected from triglycerides, free fatty acids, and fatty acid esters (such as fatty acid esters of hydroxyalkanes or of dihydroxyalkanes) and derivatives thereof, individually or in combination. Preferably the surfactant is a non-ionic surfactant or a mixture of non-ionic surfactants. The invention is also characterized as optionally including a hydrophilic component, for instance a hydroxyalkane such as ethanol and/or a polyethylene glycol having an average molecular weight of less than or equal to 1000."

And at page 6, lines 8-12, the specification states,

". . . combinations or mixtures of a hydrophobic component, a surfactant and a hydrophilic component (when used) with the water insoluble drug are necessary to obtain a stable microemulsion preconcentrate that would yield upon mixing with an aqueous medium a stable dispersion with an average particle size of between about 10 nm and about 10 microns."

The specification states at page 3, line 10,

". . . the preconcentrate of a true microemulsion is usually non-aqueous . . .".

At page 4, lines 1-3, the specification states,

". . . described are self-emulsifying preconcentrates that disperse, without the input of high energy (i.e., other than mixing energy to cause dispersion), to form droplets of average size of up to about 10 microns."

At page 7, lines 26-31, the specification states,

"An experiment to test the efficiency of forming microemulsions from the preconcentrates was carried out by diluting the preconcentrate in 20-50 fold with water or simulated gastric fluid with gentle mixing or shaking. The aqueous medium temperature varied between 20 and 37°C. Particle size analysis was then carried out using a photon correlation spectroscopy based particle sizer, Nicomp 370. Data reported in the following examples correspond to volume weighted particle size".

Originally filed claim 8 contains the following description wherein the preconcentrate must be mixed with an aqueous medium to give a microemulsion,

"8. A storage-stable self-emulsifying preconcentrate of an anticancer drug in a microemulsion composed of:

10-80% w/w of a hydrophobic component of at least one triglyceride, diglyceride, monoglyceride, free fatty acid, fatty acid ester, fish oil, vegetable oil or mixtures thereof;

20-80% w/w of surfactant phase comprising at least one non-ionic surfactant,

0-35% w/w diethylene glycol monoethylether, and

0-40% w/w of at least one hydrophilic component selected from a hydroxyalkane, dihydroxyalkane, a polyethylene glycol having an average molecular weight of at most 1000, and mixtures thereof wherein said preconcentrate, when mixed with an aqueous medium, gives an average particle size of at most 10 microns" (emphasis added).

As discussed at the interview, Applicants have provided the requested clarification of "preconcentrate" in order to overcome the rejection of the claims. Additionally, claims 45, 51, and 53 have been amended to refer to 6% to 40% of a hydrophilic component, as suggested by the Examiner. Accordingly, Applicants submit that claims 26-53 are in condition for allowance. Claims 54-57 are also patentable over the cited references.

It is believed this response summarizes all the issues discussed during the interview. Should there remain any issues outstanding, the Examiner is invited to call the undersigned at his Washington, D.C. office.

Respectfully submitted,

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Date: April 17, 2003
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RESPONSE UNDER 37 CFR 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1615

PATENT
Attorney Docket No. 402076/SKYEPHARMA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

PARIKH et al.

Application No. 09/281,430 Art Unit: 1615

Filed: March 30, 1999 Examiner: T. Ware

For: ANTICANCER COMPOSITIONS

AMENDMENTS TO CLAIMS MADE IN RESPONSE TO OFFICE ACTION DATED DECEMBER 18, 2002

Amendments to existing claims:

27. (Amended) The self-emulsifying preconcentrate of claim 26, wherein the carrier system ~~contains~~ consists of 15 to 75% w/w of the hydrophobic component.

28. (Amended) The self-emulsifying preconcentrate of claim 26, wherein the carrier system ~~contains~~ consists of up to 30% w/w of the hydrophilic component.

30. (Amended) The preconcentrate of claim 29, wherein the hydrophilic component ~~comprises~~ is selected from the group consisting of 1,2-propylene glycol and ethanol.

35. (Amended) The preconcentrate of claim ~~34~~ 29, wherein the preconcentrate comprises grapefruit extract or a component thereof.

45. (Amended) A storage-stable, self-emulsifying, and non-aqueous preconcentrate of a taxane in a microemulsion comprising a taxane dissolved in a carrier system, which carrier system consists essentially of:

10 to 80% w/w of a hydrophobic component;

20 to 80% w/w of a surfactant component; and

~~up~~6% to 40% w/w of a hydrophilic component, at least a portion of which hydrophilic component consists of ethanol, such that the carrier system contains at least 6% w/w ethanol.

51. (Amended) A storage-stable, self-emulsifying, and non-aqueous preconcentrate of a taxane in a microemulsion comprising a taxane dissolved in a carrier system, which carrier system consists essentially of:

10 to 80% w/w of a hydrophobic component selected from the group consisting of a triglyceride, a diglyceride, a monoglyceride, a free fatty acid, a fatty acid ester, a fish oil, a vegetable oil, and combinations thereof;

20 to 80% w/w of a surfactant component consisting of one or more surfactants selected from the group consisting of a polyoxyethylene-sorbitan-fatty acid ester, a polyoxyethylene fatty acid ester, a polyoxyethylene castor oil derivative, α-tocopherol, α-tocopheryl polyethylene glycol succinate, α-tocopherol palmitate, α-tocopherol acetate, a PEG glyceryl fatty acid ester, a propylene glycol mono- or di-fatty acid ester, a sorbitan fatty acid ester, a polyoxyethylene-polyoxypropylene co-polymer, glycerol triacetate, a monoglyceride, an acetylated monoglyceride, and combinations of any thereof; and

~~up~~6% to 40% of a hydrophilic component, at least a portion of the hydrophilic component consisting of ethanol, such that the carrier system contains at least 6% w/w ethanol.

53. (Amended) An injectable pharmaceutically acceptable composition consisting essentially of a storage-stable, self-emulsifying, and non-aqueous preconcentrate of at least one taxane in a composition consisting essentially of:

10 to 80% w/w of a hydrophobic component;

20 to 80% w/w of a surfactant component; and

~~up~~6% to 40% w/w of a hydrophilic component,

wherein (a) at least a portion of which hydrophilic component consists of ethanol, such that the composition contains at least 6% w/w ethanol, (b) the surfactant component of the composition consists of one or more non-ionic surfactants, or (c) ~~both~~ conditions (a) and (b) apply.